

That Which Is Claimed Is:

1. A method of detecting DNA hybridization comprising:
 - (a) contacting a DNA sample with an oligonucleotide probe to form a hybridized DNA;
 - (b) reacting said hybridized DNA with a transition metal complex capable of oxidizing a preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having at least one of said preselected bases;
 - (c) detecting said oxidation-reduction reaction;
 - (d) determining the presence or absence of hybridized DNA from said detected oxidation-reduction reaction at said preselected base.
- 5 2. The method according to Claim 1, wherein said determining step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded DNA; and then (iii) determining whether said measured reaction rate is essentially the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded DNA.
- 10 3. The method according to Claim 1, wherein said DNA sample is a single-stranded DNA sample, and said hybridized DNA is a duplex.
4. The method according to Claim 1, wherein said oligonucleotide probe includes from about 4 to about 100 bases.
5. The method according to Claim 1, wherein said preselected base is guanine.
6. The method according to Claim 1, wherein said preselected base is adenine.

7. The method according to Claim 1, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{2+}$, $\text{Fe}(\text{5-Cl-phen})_3^{2+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$:

8. The method according to Claim 1, wherein said reacting step comprises reacting said transition metal complex with said hybridized DNA sample under conditions sufficient to effect the selective oxidation of said preselected base.

9. The method according to Claim 1, further comprising the step of amplifying said hybridized DNA prior to said contacting step.

10. The method according to Claim 9, wherein said step of amplifying said DNA sample is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

11. The method according to Claim 2, wherein said step of measuring the reaction rate of said oxidation-reduction reaction comprises measuring the cyclic voltammogram of the reaction.

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12. The method according to Claim 2, wherein said step of comparing comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized DNA sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded DNA.

13. The method according to Claim 1, wherein said oligonucleotide probe is immobilized on a solid surface.

14. The method according to Claim 13, wherein said transition metal complex is immobilized on said solid surface.

15. The method according to Claim 1, further comprising the step of (e) identifying the base paired with said preselected base.

16. The method according to Claim 1, further comprising the step of (e) identifying the base paired with the base adjacent to the preselected base.

17. The method according to Claim 15 or 16, wherein said identifying step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with a DNA having adenine, cytosine, guanine, or thymine bound to said preselected base; and (iii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

18. A method of detecting DNA hybridization comprising:
(a) contacting a DNA sample with an oligonucleotide probe to form a hybridized DNA;
(b) reacting said hybridized DNA with a transition metal complex capable of oxidizing a preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having at least one of said preselected bases;
(c) detecting said oxidation-reduction reaction;
(d) measuring the reaction rate of said detected oxidation-reduction reaction;
(e) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded DNA; and then
(f) determining whether said measured reaction rate is the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded DNA.

19. The method according to Claim 18, wherein said preselected base is guanine.

20. The method according to Claim 18, wherein said preselected base is adenine.

21. The method according to Claim 18, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{3+}$, $\text{Fe}(\text{5-Cl-phen})_3^{3+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

22. The method according to Claim 18, wherein said reacting step comprises contacting said transition metal complex with said DNA sample under conditions sufficient to effect the selective oxidation of said preselected base.

23. The method according to Claim 18, further comprising the step of amplifying said DNA prior to said reacting step.

24. The method according to Claim 23, wherein said step of amplifying said hybridized DNA is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

25. The method according to Claim 18, wherein said measuring step comprises measuring the cyclic voltammogram of said reaction.

26. The method according to Claim 18, wherein said comparing step comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized DNA sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded DNA.

27. The method according to Claim 18, wherein said oligonucleotide probe is immobilized on a solid surface.

28. The method according to Claim 27, wherein said transition metal complex is immobilized on said solid surface.

29. The method according to Claim 18, further comprising the step of (g) identifying the base paired with said preselected base.

30. The method according to Claim 29, wherein said step (g) of identifying the base comprises (i) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with a DNA having adenine, cytosine, guanine, or thymine bound to said preselected base; and (ii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

31. An apparatus for detecting DNA hybridization comprising:
(a) a plurality of DNA sample containers;
(b) sample handling means for carrying said plurality of DNA sample containers;
5 (c) oligonucleotide probe delivery means for delivering said oligonucleotide probe to each of said DNA sample containers;
(d) transition metal complex delivery means for delivering said transition metal complex to each of said plurality of DNA sample containers; and
10 (e) an oxidation-reduction reaction detector for detecting an oxidation-reduction reaction.

32. The apparatus according to Claim 31, further comprising a means for measuring the oxidation-reduction reaction rate of said detected oxidation-reduction reaction.

33. The apparatus according to Claim 31, wherein said oxidation-reduction reaction detector comprises an electrode.

34. The apparatus according to Claim 31, wherein said oligonucleotide probe delivery means comprises a solid surface having said oligonucleotide probe immobilized thereon.

35. An apparatus for detecting DNA hybridization comprising:

(a) a DNA sample container;

(b) oligonucleotide probe delivery means for delivering a plurality of oligonucleotide probes to said DNA sample container;

5 (c) transition metal complex delivery means for delivering said transition metal complex to said DNA sample container; and

(d) an oxidation-reduction reaction detector for detecting an oxidation-reduction reaction.

36. The apparatus according to Claim 35, further comprising a means for measuring the oxidation-reduction reaction rate of said detected oxidation-reduction reaction.

37. The apparatus according to Claim 35, wherein said oxidation-reduction reaction detector comprises an electrode.

38. The apparatus according to Claim 35, wherein said oligonucleotide probe delivery means comprises a solid surface having a plurality of oligonucleotide probes immobilized thereon, wherein each of said oligonucleotide probes is different from the other.

39. The apparatus according to Claim 38, wherein said transition metal complex delivery means comprises said solid surface having both a plurality of oligonucleotide probes and said transition metal complex immobilized thereon.

40. A method of sequencing DNA comprising

(a) contacting a DNA sample with an oligonucleotide probe to form a hybridized DNA, said oligonucleotide probe including a preselected base having a unique oxidation rate;

5 (b) reacting said hybridized DNA with a transition metal complex capable of oxidizing said preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having a predetermined number of said preselected bases;

(c) detecting said oxidation-reduction reaction;

10 (d) measuring the reaction rate of said detected oxidation-reduction reaction; and

(e) identifying the base paired with said preselected base.

41. The method according to Claim 40, wherein said identifying step comprises (i) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with a DNA having adenine, cytosine, guanine, or thymine bound to said preselected base; and (ii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

5 42. The method according to Claim 40, wherein said oligonucleotide probe further includes a second preselected base having a unique oxidation rate, wherein the oxidation rate of said second preselected base is different from the oxidation rate of said preselected base.

43. The method according to Claim 42, wherein said detecting step further comprises detecting the oxidation-reduction reaction of the transition metal complex with said second preselected base; wherein said measuring step further comprises measuring the reaction rate of said detected oxidation-reduction reaction of the transition metal complex with said second preselected base; and wherein said identifying step further comprises identifying the base paired with said second preselected base.

44. The method according to Claim 40, further comprising repeating steps (a) through (e) with a sufficient number of oligonucleotide probes having said preselected base at different sites to identify each base in said DNA sample.

45. A method of detecting RNA hybridization comprising:

(a) contacting an RNA sample with an oligonucleotide probe to form a hybridized RNA;

5 (b) reacting said hybridized RNA with a transition metal complex capable of oxidizing a preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having at least one of said preselected bases;

(c) detecting said oxidation-reduction reaction;

(d) determining the presence or absence of hybridized RNA from 10 said detected oxidation-reduction reaction at said preselected base.

46. The method according to Claim 45, wherein said determining step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded RNA; and then (iii) determining whether said measured reaction rate is essentially the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded RNA.

47. The method according to Claim 45, wherein said RNA sample is a single-stranded RNA sample, and said hybridized RNA is a duplex.

48. The method according to Claim 45, wherein said oligonucleotide probe includes from about 4 to about 100 bases.

49. The method according to Claim 45, wherein said preselected base is guanine.

50. The method according to Claim 45, wherein said preselected base is adenine.

51. The method according to Claim 45, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{2+}$, $\text{Fe}(\text{5-Cl-phen})_3^{2+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

52. The method according to Claim 45, wherein said reacting step comprises reacting said transition metal complex with said hybridized RNA sample under conditions sufficient to effect the selective oxidation of said preselected base.

53. The method according to Claim 45, further comprising the step of amplifying said hybridized RNA prior to said contacting step.

54. The method according to Claim 53, wherein said step of amplifying said RNA sample is carried out by reverse-transcriptase polymerase chain reaction.

55. The method according to Claim 46, wherein said step of measuring the reaction rate of said oxidation-reduction reaction comprises measuring the cyclic voltammogram of the reaction.

56. The method according to Claim 46, wherein said step of comparing comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized RNA sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded RNA.

57. The method according to Claim 45, wherein said oligonucleotide probe is immobilized on a solid surface.

58. The method according to Claim 57, wherein said transition metal complex is immobilized on said solid surface.

59. The method according to Claim 45, further comprising the step of (e) identifying the base paired with said preselected base.

60. The method according to Claim 45, further comprising the step of (e) identifying the base paired with the base adjacent to the preselected base.

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61. The method according to Claim 59 or 60, wherein said identifying step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with an RNA having adenine, cytosine, guanine, or uracil bound to said preselected base; and (iii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

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62. A method of detecting RNA hybridization comprising:
(a) contacting an RNA sample with an oligonucleotide probe to form a hybridized RNA;

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(b) reacting said hybridized RNA with a transition metal complex capable of oxidizing a preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having at least one of said preselected bases;

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(c) detecting said oxidation-reduction reaction;
(d) measuring the reaction rate of said detected oxidation-reduction reaction;

(e) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded RNA; and then

15 (f) determining whether said measured reaction rate is the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded RNA.

63. The method according to Claim 62, wherein said preselected base is guanine.

64. The method according to Claim 62, wherein said preselected base is adenine.

65. The method according to Claim 62, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{3+}$, $\text{Fe}(\text{5-Cl-phen})_3^{3+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

66. The method according to Claim 62, wherein said reacting step comprises contacting said transition metal complex with said RNA sample under conditions sufficient to effect the selective oxidation of said preselected base.

67. The method according to Claim 62, further comprising the step of amplifying said RNA prior to said reacting step.

68. The method according to Claim 67, wherein said step of amplifying said hybridized RNA is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

69. The method according to Claim 62, wherein said measuring step comprises measuring the cyclic voltammogram of said reaction.

70. The method according to Claim 62, wherein said comparing step comprises comparing the cyclic voltammogram of the reaction of the transition

metal complex with the hybridized RNA sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded RNA.

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71. The method according to Claim 62, wherein said oligonucleotide probe is immobilized on a solid surface.

72. The method according to Claim 71, wherein said transition metal complex is immobilized on said solid surface.

73. The method according to Claim 62, further comprising the step of (g) identifying the base paired with said preselected base.

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74. The method according to Claim 73, wherein said step (g) of identifying the base comprises (i) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with an RNA having adenine, cytosine, guanine, or uracil bound to said preselected base; and (ii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

75. A method of sequencing RNA comprising:

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(a) contacting an RNA sample with an oligonucleotide probe to form a hybridized RNA, said oligonucleotide probe including a preselected base having a unique oxidation rate;

(b) reacting said hybridized RNA with a transition metal complex capable of oxidizing said preselected base in said oligonucleotide probe in an oxidation-reduction reaction, said oligonucleotide probe having a predetermined number of said preselected bases;

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(c) detecting said oxidation-reduction reaction;

(d) measuring the reaction rate of said detected oxidation-reduction reaction; and

(e) identifying the base paired with said preselected base.

76. The method according to Claim 75, wherein said identifying step comprises (i) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with an RNA having adenine, cytosine, guanine, or uracil bound to said preselected base; and (ii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

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77. The method according to Claim 75, wherein said oligonucleotide probe further includes a second preselected base having a unique oxidation rate, wherein the oxidation rate of said second preselected base is different from the oxidation rate of said preselected base.

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78. The method according to Claim 77, wherein said detecting step further comprises detecting the oxidation-reduction reaction of the transition metal complex with said second preselected base; wherein said measuring step further comprises measuring the reaction rate of said detected oxidation-reduction reaction of the transition metal complex with said second preselected base; and wherein said identifying step further comprises identifying the base paired with said second preselected base.

79. The method according to Claim 75, further comprising repeating steps (a) through (e) with a sufficient number of oligonucleotide probes having said preselected base at different sites to identify each base in said RNA sample.

80. A method of detecting a nucleic acid, said nucleic acid containing at least one preselected base, said method comprising:

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(a) reacting said nucleic acid with a transition metal complex capable of oxidizing said preselected base in an oxidation-reduction reaction;

(b) detecting said oxidation-reduction reaction; and

(c) determining the presence or absence of said nucleic acid from said detected oxidation-reduction reaction at said preselected base.

81. A method according to claim 80, wherein said reacting step is preceded by the step of:

contacting said nucleic acid with a complementary nucleic acid to form a hybridized nucleic acid.

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82. The method according to Claim 81, wherein said determining step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded nucleic acid; and then (iii) determining whether said measured reaction rate is essentially the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded nucleic acid.

83. The method according to Claim 82, wherein said step of measuring the reaction rate of said oxidation-reduction reaction comprises measuring the cyclic voltammogram of the reaction.

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84. The method according to Claim 82, wherein said step of comparing comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized nucleic acid sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded nucleic acid.

85. The method according to Claim 81, wherein said determining step is followed by the step of:

identifying the base paired with said preselected base.

86. The method according to Claim 81, wherein said determining step is followed by the step of:

identifying the base paired with the base adjacent to the preselected base.

87. The method according to Claim 85 or 86, wherein said identifying step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to each of the five different known oxidation-reduction reaction rates of the transition metal complex with a nucleic acid having adenine, cytosine, guanine, thymine, or uracil bound to said preselected base; and (iii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

88. The method according to Claim 80, wherein said nucleic acid includes from about 4 to about 100 bases.

89. The method according to Claim 80, wherein said preselected base is selected from the group consisting of guanine and adenine.

90. The method according to Claim 80, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{2+}$, $\text{Fe}(\text{5-Cl-phen})_3^{2+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

91. A method according to claim 80, wherein said nucleic acid is DNA.

92. A method according to claim 80, wherein said nucleic acid is RNA.

93. The method according to Claim 80, wherein said reacting step comprises reacting said transition metal complex with said nucleic acid under conditions sufficient to effect the selective oxidation of said preselected base.

94. The method according to Claim 80, further comprising the step of amplifying said nucleic acid prior to said reacting step.

95. The method according to Claim 94, wherein said step of amplifying said nucleic acid is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

96. The method according to Claim 80, wherein said nucleic acid is immobilized on a solid surface.

97. The method according to Claim 96, wherein said transition metal complex is immobilized on said solid surface.

98. A method of detecting the presence or absence of a target nucleic acid in a test sample suspected of containing the same, wherein said target nucleic acid contains at least one preselected base, said method comprising:

5 (a) contacting said test sample to an oligonucleotide probe that specifically binds said to said target nucleic acid to form a hybridized nucleic acid;

(b) contacting said hybridized nucleic acid to a transition metal complex that oxidizes said preselected base in an oxidation-reduction reaction;

(c) detecting the presence or absence of said oxidation-reduction reaction associated with said hybridized nucleic acid; and

10 (d) determining the presence or absence of said target nucleic acid in said test sample from said detected oxidation-reduction reaction at said preselected base.

99. A method according to claim 98, further comprising the step of:

separating said test sample from said hybridized nucleic acid prior to said detecting step.

100. A method according to claim 98, wherein said target nucleic acid contains at least ten more of said preselected base than said oligonucleotide probe.

101. A method according to claim 98, wherein said oligonucleotide probe is free of said preselected base.

102. A method according to claim 98, wherein said target nucleic acid is longer than said oligonucleotide probe, and wherein at least one of said preselected base is not hybridized to said oligonucleotide probe in said hybridized nucleic acid.

103. A method according to claim 98, wherein said determining step is a quantitatively determining step.

104. The method according to Claim 98, wherein said determining step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded target nucleic acid; and then (iii) determining whether said measured reaction rate is essentially the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded target nucleic acid.

105. The method according to Claim 104, wherein said step of measuring the reaction rate of said oxidation-reduction reaction comprises measuring the cyclic voltammogram of the reaction.

106. The method according to Claim 104, wherein said step of comparing comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized target nucleic acid sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded target nucleic acid.

107. The method according to Claim 98, wherein said target nucleic acid includes from about 4 to about 100 bases.

108. The method according to Claim 98, wherein said preselected base is selected from the group consisting of guanine and adenine.

109. The method according to Claim 98, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{2+}$, $\text{Fe}(\text{5-Cl-phen})_3^{2+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

110. A method according to claim 98, wherein said target nucleic acid is DNA.

111. A method according to claim 98, wherein said target nucleic acid is RNA.

112. The method according to Claim 98, wherein said reacting step comprises reacting said transition metal complex with said target nucleic acid under conditions that effect the selective oxidation of said preselected base.

113. The method according to Claim 98, further comprising the step of amplifying said target nucleic acid prior to said reacting step.

114. The method according to Claim 113, wherein said step of amplifying said target nucleic acid sample is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

115. The method according to Claim 98, wherein said oligonucleotide probe is immobilized on a solid surface.

116. The method according to Claim 115, wherein said transition metal complex is immobilized on said solid surface.

117. A method of detecting a target nucleic acid, said target nucleic acid containing at least one preselected base, said method comprising:

5 (a) contacting said target nucleic acid to a complementary nucleic acid that specifically binds to said target nucleic acid to form a hybridized nucleic acid;

(b) reacting said hybridized nucleic acid with a transition metal complex capable of oxidizing said preselected base in an oxidation-reduction reaction;

10 (c) detecting said oxidation-reduction reaction; and

(d) determining the presence or absence of said nucleic acid from said detected oxidation-reduction reaction at said preselected base;

wherein said preselected base in said target nucleic acid is guanine; said target nucleic acid contains cytosine, and said complementary nucleic acid contains an alternate base that bonds to cytosine in said hybridized nucleic acid;

15 and wherein said alternate base is selected from the group consisting of inosine and 7-deaza-guanine.

118. The method according to Claim 117, wherein said reacting step comprises reacting said transition metal complex with said nucleic acid under conditions sufficient to effect the selective oxidation of said preselected base without oxidizing said alternate base.

119. The method according to Claim 117, wherein said determining step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to the oxidation-reduction reaction rate of the transition metal complex with a single-stranded nucleic acid; and then (iii) determining whether said measured reaction rate is essentially the same as the oxidation-reduction reaction rate of the transition metal complex with single-stranded nucleic acid.

120. The method according to Claim 119, wherein said step of measuring the reaction rate of said oxidation-reduction reaction comprises measuring the cyclic voltammogram of the reaction.

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121. The method according to Claim 119, wherein said step of comparing comprises comparing the cyclic voltammogram of the reaction of the transition metal complex with the hybridized nucleic acid sample against the known cyclic voltammogram of the reaction of the transition metal complex with single-stranded nucleic acid.

122. The method according to Claim 117, wherein said determining step is followed by the step of:

identifying the base paired with said preselected base.

123. The method according to Claim 117, wherein said determining step is followed by the step of:

identifying the base paired with the base adjacent to the preselected base.

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124. The method according to Claim 122 or 123, wherein said identifying step further comprises the steps of: (i) measuring the reaction rate of said detected oxidation-reduction reaction, (ii) comparing said measured reaction rate to each of the four different known oxidation-reduction reaction rates of the transition metal complex with a nucleic acid having adenine, cytosine, guanine, thymine, or uracil bound to said preselected base; and (iii) determining which of said known oxidation-reduction reaction rates is essentially the same as said measured reaction rate.

125. The method according to Claim 117, wherein said target nucleic acid includes from about 4 to about 100 bases.

126. The method according to Claim 117, wherein said transition metal complex is selected from the group consisting of $\text{Ru}(\text{bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-bpy})_3^{2+}$, $\text{Ru}(\text{Me}_2\text{-phen})_3^{2+}$, $\text{Fe}(\text{bpy})_3^{2+}$, $\text{Fe}(\text{5-Cl-phen})_3^{2+}$, $\text{Os}(\text{bpy})_3^{2+}$, $\text{Os}(\text{5-Cl-phen})_3^{2+}$, and $\text{ReO}_2(\text{py})_4^{1+}$.

127. A method according to claim 117, wherein said target nucleic acid is DNA.

128. A method according to claim 117, wherein said target nucleic acid is RNA.

129. The method according to Claim 117, further comprising the step of amplifying said target nucleic acid prior to said reacting step.

130. The method according to Claim 129, wherein said step of amplifying said target nucleic acid is carried out by polymerase chain reaction, strand displacement amplification, ligase chain reaction, or nucleic acid sequence-based amplification.

131. The method according to Claim 117, wherein said complementary nucleic acid is immobilized on a solid surface.

132. The method according to Claim 131, wherein said transition metal complex is immobilized on said solid surface.

133. A method of detecting the presence or absence of a target nucleic acid in a test sample suspected of containing the same, said method comprising:

5 (a) contacting said test sample to an oligonucleotide probe that specifically binds said to said target nucleic acid to form a hybridized nucleic acid, said oligonucleotide probe having end terminals that are blocked for elongation by terminal transferase;

10 (b) contacting said hybridized nucleic acid to a solution containing a preselected base in the presence of terminal transferase to produce an extension product of said target nucleic acid, with said extension product comprised of said preselected base;

(c) contacting said oligonucleotide probe to a transition metal complex that oxidizes said preselected base in an oxidation-reduction reaction;

15 (d) detecting the presence or absence of said said oxidation-reduction reaction; and

(e) determining the presence or absence of said target nucleic acid in said test sample from said detected oxidation-reduction reaction at said preselected base.

134. A method according to claim 133, further comprising the step of:

separating said test sample from said hybridized nucleic acid prior to said detecting step.

135. A method of detecting the presence or absence of a target nucleic acid in a test sample suspected of containing the same, said method comprising:

5 (a) providing an oligonucleotide capture probe, wherein said capture probe specifically binds to said target nucleic acid;

(b) contacting said test sample to said capture probe to form a hybridized nucleic acid;

10 (c) contacting an oligonucleotide signal probe to said hybridized nucleic acid, wherein said signal probe specifically binds to said target nucleic acid therein, and wherein said signal probe contains at least one preselected base, to produce a hybridized nucleic acid sandwich;

(d) contacting said hybridized nucleic acid sandwich to a transition metal complex that oxidizes said preselected base in an oxidation-reduction reaction;

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(e) detecting the presence or absence of said oxidation-reduction reaction associated with said hybridized nucleic acid sandwich; and

(f) determining the presence or absence of said target nucleic acid in said test sample from said detected oxidation-reduction reaction at said preselected base.

136. A method according to claim 135, further comprising the step of:

separating said test sample from said hybridized nucleic acid prior to said detecting step.

137. A method according to claim 136, wherein said separating step is carried out between step (b) and step (c), or between step (c) and step (d).

138. A microelectronic device useful for the electrochemical detection of a nucleic acid species, said device comprising:

a microelectronic substrate having first and second opposing faces;
a conductive electrode on said first face; and

5 an oligonucleotide capture probe immobilized on said first face adjacent said conductive electrode.

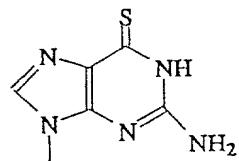
139. A microelectronic device according to claim 138, said device having a plurality of conductive electrodes on said first face and a plurality of different oligonucleotide capture probes immobilized on said first face, with each of said different oligonucleotide capture probes positioned adjacent a different conductive electrode.

5 140. A microelectronic device according to claim 138, further comprising a contact electrically connected to said conductive electrode.

141. A microelectronic device according to claim 138, wherein said substrate is silicon.

142. A microelectronic device according to claim 138, wherein said oligonucleotide capture probe is from 4 to 100 nucleotides in length.

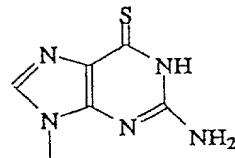
143. An oligonucleotide probe useful for the electrochemical detection of a preselected base in the presence of background guanine signal, said oligonucleotide probe including at least one purine base according to Formula I:



144. The oligonucleotide probe according to Claim 143, wherein said probe is up to 100 bases in length.

145. A method of detecting a nucleic acid, comprising:

(a) providing a nucleic acid containing at least one preselected base of the formula:



; and then

5 (b) reacting said nucleic acid with a transition metal complex capable of oxidizing said preselected base in an oxidation-reduction reaction;

(c) detecting said oxidation-reduction reaction; and

(d) determining the presence or absence of said nucleic acid from said detected oxidation-reduction reaction at said preselected base.

146. A method according to claim 145, wherein said reacting step is preceded by the step of:

contacting said nucleic acid with a complementary nucleic acid to form a hybridized nucleic acid.

147. A method according to claim 146, wherein said complementary nucleic acid contains at least one guanine substituent therein.

148. An electrode useful for the electrochemical detection of a preselected base in a nucleic acid, by reacting said nucleic acid with a transition metal complex capable of oxidizing said preselected base in an oxidation-reduction reaction, said electrode comprising:

5 (a) a conductive substrate having a working surface formed thereon; and

(b) a polymer layer connected to said working surface, wherein said polymer layer is porous to said transition metal complex, and wherein said polymer layer binds said nucleic acid thereto.

149. An electrode according to claim 148, further comprising a nucleic acid bound to said polymer layer, said nucleic containing at least one of said preselected base.

150. A method of detecting a nucleic acid, said nucleic acid containing at least one preselected base, said method comprising:

5 (a) contacting a sample containing said nucleic acid to an electrode, said electrode comprising (i) a conductive substrate having a working surface formed thereon; and (ii) a polymer layer connected to said working surface, wherein said polymer layer binds said nucleic acid thereto;

(b) reacting said nucleic acid with a transition metal complex capable of oxidizing said preselected base in an oxidation-reduction reaction, and wherein said polymer layer is porous to said transition metal complex;

10 (c) detecting said oxidation-reduction reaction by measuring current flow through said electrode; and

(d) determining the presence or absence of said nucleic acid from said detected oxidation-reduction reaction at said preselected base.

151. A method according to claim 150, wherein said reacting step is preceded by the step of:

contacting said nucleic acid with a complementary nucleic acid to form a hybridized nucleic acid.